

Some effects of gram-negative bacterial endotoxin and its importance as a contaminator of biological preparations.

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The purpose of this study was to establish a model which can be used to examine the biological response to Salmonella typhimurium endotoxin in both anaesthetized and unanaesthetized rabbits, and then compare this response to that of rabbits injected with an endotoxin-contaminated biological preparation. The parameters used to evaluate the biological response included total white blood cell and differential counts, 15-ketodihydro-PGF2 alpha concentration, and rectal temperature. Unanaesthetized groups of rabbits received 1000, 100, 10, or 1 ng/kg of the endotoxin via intravenous injection (i.v.); the anaesthetized group of rabbits received 100 ng/kg endotoxin i.v. (anaesthesia induced with Hypnorm). In addition, groups of rabbits were treated under anaesthesia with Pharmacia-Chiron's recombinant human Cu/Zn superoxide dismutase (SOD) (10 mg/kg body weight = 1.6 endotoxin units (EU)/kg) or Grunenthal's bovine SOD (two doses: 10 mg/kg = 400 EU/kg, or 50 mg/kg = 2000 EU/kg). Results demonstrated that at the lower doses of endotoxin (10 and 1 ng/kg) and r-hSOD (10 mg/kg), no leukopenia was observed. There was however a slight shift in the leukocyte population so that polymorphonucleocytes increased and monocytes decreased in number. Rabbits treated with higher doses of endotoxin (1000 and 100 ng/kg) showed many of the common signs of endotoxemia, including leukopenia, increased prostaglandin metabolite levels, and increased body temperature, as did the rabbits treated with endotoxincontaminated bSOD. There was a definite dose-dependency, with the higher dose of bSOD giving a more marked rise in all parameters. These findings indicate that use of this or other endotoxin-contaminated biological preparations in live-animal experiments could produce erratic, and therefore unreliable, results.

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